c] pyridinyl and $R_2$ is $SO_2$-phenyl or $SO_2$-naphthyl in combination with at least one other agent selected from diagnostic agents, cardioprotective agents, direct thrombin inhibiting agents, anticoagulant agent, antiplatelet agents and fibrinolytic agents, classified in classes 514 and 546 among various subclasses depending upon substituents.

II. Claims 35-41(in part) drawn to a method of treatment using compounds of Formula I and pharmaceutical compositions thereof in which $Ar^1$ is pyrrolo [2,3-c] pyridinyl and $R_2$ is $SO_2$-(5-membered heteroaryl or heterocyclyl) in combination with the aforementioned agents of Group I, classified in classes 514 and 546 among various subclasses depending upon substituents.

III. Claims 35-41 (in part) drawn to a method of treatment using compounds of Formula I and pharmaceutical compositions thereof in which $Ar^1$ is pyrrolo [2,3-c] pyridinyl and $R_2$ is $SO_2$-(6-member heteroaryl) in combination with the aforementioned agents of Group I, classified in classes 514 and 546 among various subclasses depending upon substituents.

IV. Claims 35-41 (in part) drawn to a method of treatment using compounds of Formula I and pharmaceutical compositions thereof in which $Ar^1$ is pyrrolo [2,3-c] pyridinyl and $R_2$ is $SO_2$-quinolinyl in combination with the aforementioned agents of Group I, classified in classes 514 and 546 among various subclasses depending upon substituents.

V. Claims 35-41 (in part) drawn to a method of treatment using compounds of Formula I and pharmaceutical compositions thereof in which $Ar^1$ is pyrrolo [2,3-c] pyridinyl and $R_2$ is $SO_2$ - benzopyranyl in combination with the aforementioned agents of Group I classified in classes 514 and 546 among various subclasses depending upon substituents.

VI. Claims 35-41 (in part) drawn to a method of treatment using compounds of Formula I and pharmaceutical compositions thereof in which $Ar^1$ is pyrrolo [2,3-b] pyridinyl and $R_2$ is $SO_2$-phenyl or $SO_2$-naphthyl in combination with the aforementioned agents of Group I, classified in classes 514 and 546 among various subclasses depending upon substituents.

VII. Claims 35-41 (in part) drawn to a method of treatment using compounds of Formula I and pharmaceutical compositions thereof in which $Ar^1$ is pyrrolo [2,3-b] pyridinyl and $R_2$ is $SO_2$-(5-membered heteroary or heterocyclyl) in combination with the aforementioned agents of Group I, classified in classes 514 and 546 among various subclasses depending upon substituents.

VIII. Claims 35-41 (in part) drawn to a method of treatment using compounds of Formula I and pharmaceutical compositions thereof in which $Ar^1$ is pyrrolo [2,3-b] pyridinyl and $R_2$ is $SO_2$ –(6-membered heteroaryl) in combination with the aforementioned agents of Group I, classified in classes 514 and 546 among various subclasses depending upon substituents.

IX. Claims 35-41 (in part) drawn to a method of treatment using compounds of Formula I and pharmaceutical compositions thereof in which $Ar^1$ is pyrrolo [2,3-b] pyridinyl and $R_2$ is $SO_2$ – quinolinyl in combination with the aforementioned agents of Group I, classified in classes 514 and 546 among various subclasses depending upon substituents.

X. Claims 35-41 (in part) drawn to a method of treatment using compounds of Formula I and pharmaceutical compositions thereof in which $Ar^1$ is pyrrolo [2,3-b] pyridinyl and R is $SO_2$-benzopyranyl in combination with the aforementioned agents of Group I classified in classes in 514 and 546 among various subclasses depending upon substituents.

XI. Claims 35-41 (in part) drawn to a method of treatment using compounds of Formula I and pharmaceutical compositions thereof in which $Ar^1$ is pyrrolo [2,3-c] pyridinyl and $R_2$ is $SO_2$-phenyl or SO – naphthyl in combination with the aforementioned agents of Group I, classified in classes in 514 and 546 among various subclasses depending upon substituents.

XII. Claims 35-41 (in part) drawn to a method of treatment using compounds of Formula I and pharmaceutical compositions thereof in which $Ar^1$ is pyrrolo [3,2-c] pyridinyl and $R_2$ is $SO_2$-(5-heteroaryl or heterocyclyl) in combination with the aforementioned agents of Group I, classified in classes 514 and 546 among various subclasses depending upon substituents.

XIII. Claims 35-41 (in part) drawn to a method of treatment using compounds of Formula I and pharmaceutical compositions thereof in which $Ar^1$ is pyrrolo [3,2-c] pyridinyl and $R_2$ is $SO_2$- (6-heteroaryl) in combination with the aforementioned agents of Group I, classified in classes in 514 and 546 among various subclasses depending upon substituents.

XIV. Claims 35-41 (in part) drawn to a method of treatment using compounds of Formula I and pharmaceutical compositions thereof in which $Ar^1$ is pyrrolo [3,2-c] pyridinyl and $R_2$ is $SO_2$-quinolinyl in combination with the aforementioned agents of Group I, classified in classes in 514 and 546 among various subclasses depending upon substituents.

XV. Claims 35-41 (in part) drawn to a method of treatment using compounds of Formula I and pharmaceutical compositions thereof in which $Ar^1$ is pyrrolo [3,2-c] pyridinyl and $R_2$ is $SO_2$-benzopyramyl in combination with the aforementioned agents of Group I, classified in classes 514 and 546 among various subclasses depending upon substituents.

XVI. Claims 35-41 (in part) drawn to a method of treatment using compounds of Formula I and pharmaceutical compositions thereof in which the combination of $Ar^1$ and $R_2$ is not in Group I-XV in, in combination with the aforementioned agents of Group I, classified in classes 514 and 546 among various subclasses depending upon substituents.

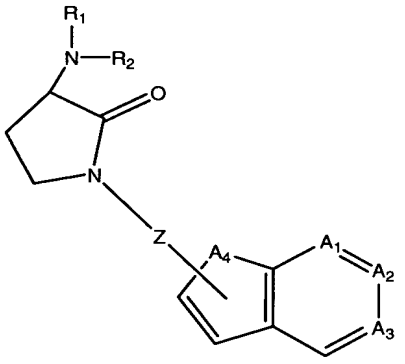
Applicants submit that the Election and Restriction Requirements are improper for dividing Applicants' Markush claim in contravention to the Requirements of MPEP § 803.02 and case law.

**MPEP § 803.02 Considerations**

In particular, MPEP § 803.02 provides that there is no basis for requiring election or restriction of a Markush claimed invention where two factors are met, i.e.,

> ... compounds included within a Markush Group (1) share a common utility and (2) share a substantial structural feature ...

Applicant's Markush claimed in meets the aforesaid factors. That is: (A) their compounds have a substantial structural feature, i.e., the formula:




(B) their compounds share a common utility, i.e., being useful for treating physiological disorders capable of being modulated by inhibiting an activity of Factor Xa. Thus, the present Election and Restriction Requirements are improper. There is also no basis for the present

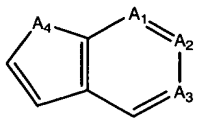
Election and Restriction Requirements because the Examiner has failed to address the above two factors of MPEP § 803.02 in making the Election and Restriction Requirements.

**Case Law Considerations**

The present Restriction Requirement is based upon variation in $R_2$ and $Ar^1$ substituents on a pyrrolidinone nucleus. In Re Harnisch, 206 U.S.P.Q. 300 (CCPA 1980) and cases related thereto, including Ex parte Dahlen and Zwilgmeyer, 42 U.S.P.Q. 208 (Bd. App. 1938), Ex parte Brouard et al., 201 U.S.P.Q. 538 (Bd. App. 1976) and Ex parte Holt and Randell, 214 U.S.P.Q. 381 (Bd. App. 1982) do not support the present Election and Restriction Requirements. In In re Harnisch, 206 U.S.P.Q. 300 ( CCPA 1980), the court reiterated that the grouping of compounds having the same nuclei but side chains wherein there was a wide variation was proper if the compounds all belong to the same genus having a community of properties justifying their grouping. In re Harnisch, 206 U.S.P.Q.at 305. The present Restriction Requirement is therefore explicitly contravened by In re Harnisch. The Examiner seeks to restrict a grouping of compounds with a common nucleus and community of properties because the Examiner considers two of the substituent groups, $R_2$ and $Ar^1$, to widely vary. However, according to In re Harnisch, this is not a proper basis for Restriction.

Furthermore, there is not even "wide variation" in the substituent group identified by the Examiner as $Ar^1$. The only possible variations of the $Ar^1$ group identified by the Examiner is three isomers of a pyrrolopyridine fused ring structure.

In addition, applicants note that there is no $Ar^1$ group in the presently pending claims for the Examiner to restrict. In the amendment submitted April 4, 2005, the $Ar^1$ group was replaced with a fused ring structure having the formula:

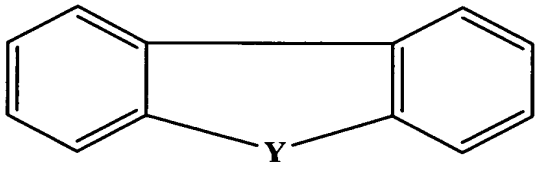


wherein one of $A_1$,$A_2$ and $A_3$ is N and the other two are CH and $A_4$ is $NR_{11}$. The purpose of replacing $Ar^1$ with this structure was to illustrate that the common nucleus having a community of properties in the claimed structure is a pyrrolidinone linked by a divalent "Z" to a pyrrolo-pyridine fused ring structure that can vary isomerically. Viewed in this manner, there is unity of invention between the two rings, so that restriction of the pyrrolopyridine ring is improper. Furthermore, because the $R_2$ group is a side chain for which wide variation is permitted pursuant to In re Harnisch, restriction of the $R_2$ group is also improper.

Nevertheless, even assuming the Examiner's identification of the pyrrolidinone ring as the common nucleus, variation among three $Ar^1$ substituents and the $R_2$ side groups does not provide an adequate basis for restriction under In re Harnisch because, despite such variation, a genus of compounds can still be identified having a community of properties that justify their grouping. Therefore, the present Election and Restriction Requirements are improper because they seek election among substituents attached to a common nucleus defining a genus of compounds with a community of properties.

Furthermore, there is no basis for the present Election and Restriction Requirements because the Examiner has failed to address the above the above Harnisch factors.

In Ex parte Dahlen and Zwilgmeyer, 42 U.S.P.Q. 208 (Bd. App. 1938), a Markush compound of the formula:




was found to be proper when Y was defined as a bivalent bridge radical that was further defined in Markush format as consisting of the following 12 members: $-CH_2-$, -CO-, -C=C-, $-CH_2CH_2-$, -NH-, -N-Alkyl-, -O-, -S-, -N=N-, -N=N-, -N=NO-, $-SO_2-$, -COCO-. Particularly noteworthy regarding that compound was that the Markush grouping was found to be acceptable even though the variable Y provided for variations in the size and classes of tricyclic ring systems, i.e., the central ring could be defined to have a ring size of 5 or 6 members that included a ring selected

from a cyclopentadienyl ring, a cyclohexadienyl ring, a phenyl ring, and one of four different heteroaryl rings (pyrrolyl, furanyl, thienyl or pyridazinyl). This demonstrates that the present restriction among pyrrolopyridinyl ring isomers is improper because it gives rise to exceptionally less variability in the classes of compounds encompassed by the genus defined by the core pyrrolidinone ring and $R_2$ and $Ar^1$ substituents. Accordingly, Applicants submit that Ex parte Dahlen and Zwilgmeyer supports that there is no basis for Election or Restriction in the instant case even though there is variability among pyrrolopyridine fused ring isomers.

Furthermore, Ex parte Brouard et al., 201 U.S.P.Q. 538(Bd. App. 1976) state that " ... the fact that different fields of search are involved does not establish that the Markush group is improper." In particular, six different fields of search were not sufficient in Ex parte Brouard et al., to establish a proper Election or Restriction of the Markush group therein. Likewise, because there are only two different fields (514 and 546) related to the presently restricted groups I-XVI of the invention, this should not be viewed as providing the proper basis of support for either Election or Restriction.

In view of the aforesaid, Applicants submit that Applicant's invention is not properly subject to Restriction or Election.

Applicants also submit that the applicable standard under which claims subject to Restriction are evaluated should not include whether there would be a serious burden on the Examiner were Restriction not required, as suggested by MPEP § 803.[1] Rather, the standard should align with the holding of In re Harnisch, 206 U.S.P.Q. 300 (CCPA 1980).

[1] See MPEP § 803, Restriction-When Proper states: "Under the statute an application may properly be required to be restricted to one of two or more claimed inventions only if they are able to support separate patents and they are either independent (MPEP § 806.04-§ 806.04(i) or distinct (MPEP § 806.05 – § 806.05(i)). If the search and examination can be made without serious burden, the Examiner must examine it on the merits, even though it includes claims to independent or distinct inventions. CRITERIA FOR RESTRICTION BETWEEN PATENTABLY DISTINCT INVENTIONS. There are two criteria for proper requirement for restriction between patentably distinct inventions: (A) The inventions must be independent (See MPEP § 802.01, § 806.04, § 808.01) or distinct as claimed (See MPEP § 806.05- § 806.05(i)); and (B) There must be a serious burden on the Examiner if Restriction is required (See MPEP § 803.02, § 806.04(a) – § 806.04(i), § 808.01(a), and § 808.02)."

Not only has the Examiner disregarded In re Harnisch and related cases such as Ex parte Dahlen and Zwilgmeyer, 42 U.S.P.Q. 208 and Ex parte Brouard et al. 201 U.S.P.Q. 538, but the present Election and Restriction Requirements directly contravene the holding of Ex parte Holt and Randell, 214 U.S.P.Q. 381.

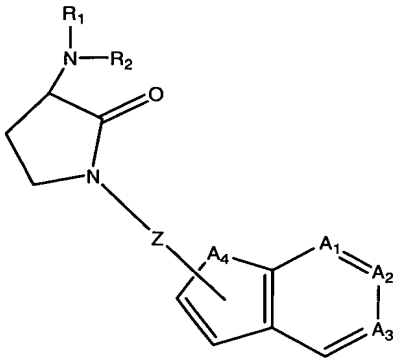
The PTO Board Appeals in Ex parte Holt and Randell, 214 U.S.P.Q. 381, held that there is no basis for a Markush Rejection where "the Examiner dissects the molecule into core and pendent substituents and then concludes that variable cores inherently constituted an improper Markush group." Id. at 386. This holding is supported by Harnisch language that requires a Markush grouping analysis be conducted based upon a molecule "as a whole," and not as a separately dissected parts of an invention, or separately dissected sections of claims when analyzing Markush-type claims.

In the instant case, the Examiner has: (1) misidentified the common structural feature pyrrolidinone as being the "core" of Applcants' claimed invention; (2) inappropriately truncated a common structural feature (pyrrolopyridine) that Applicants submit is also part of the "core" of their claimed invention; and (3) based the Restriction solely on substituents on the misidentified common structure (i.e., substituents that are actually part of the common structural core serve as the basis for the Restriction.)

Regarding the misidentified core, the Examiner states, "all groups share the ring of *pyrrolidinone* [emphasis by Examiner]." See Office Action at page 9. However, Applicants submit their claimed compounds are not pyrrolidinones, but in fact are pyrrolidinone-pyrrolopyridines.

Consequently, the Examiner has misdirected the basis for the search and Restriction Requirement by dissecting the molecule into a smaller core and pendent substituents to improperly conclude that the core of the molecule only includes a pyrrolidinone ring substituted by one of three pyrrolopyridine isomers, as well as $R_2$ substituents.

Applicants submit that the Examiner's search should have been based upon the following structural "core:"




and not just the pyrrolidinone portion of that core. Despite the $A_1$- $A_4$ variation within the pyrrolopyridine portion of the core, as well as the "Z" bridge variation between pyrrolidinone and pyrrolopyridine rings, a search based upon this structural core will not present an undue burden to the Examiner. As the Examiner acknowledges, there are only two classes in which compounds having this core are classified.

In summary, the pyrrolopyridine ring is part of the common structural core claimed and not a substituent subject to Restriction. Even if it were a substituent, the three isomers claimed do not vary so widely as to prohibit their grouping pursuant to In re Harnisch. Finally, because $R_2$ is a substituent of the core ring identified by the Examiner, and because variation among the $R_2$ groups does not affect the common properties of the compounds claimed, Restriction among the $R_2$ groups is also improper pursuant to In re Harnisch.

In view of the aforesaid comments regarding MPEP § 803.02 and case law cited by Applicants, Applicants request that Applicants' arguments regarding the impropriety of the Election and Restriction Requirements be specifically addressed on both the bases of MPEP § 803.02 and case law if the Election and Restriction Requirements are maintained. Furthermore, Applicants request they be provided with the opportunity to respond to any new bases made in support of the Election and Restriction Requirements before the Election and Restriction Requirements are made final.

***Provisional Election***

To comply with the Examiner's Election Requirements, Applicant provisionally elect, with traverse, Group XVI, and elect as the species within that group thieno[3,2-b] pyridine-2-sulfonic acid [2-oxo-1-(1 H-pyrrolo[2,3-c]pyryidin-2-ylmethyl)-pyrrolidin-3-(S)-yl]-amide. The elected species is depicted in Example 48. Applicants affirm their right to file one or more Divisional Applications with respect to any of the non-elected subject matter.

If there are any additional charges in connection with this response, the Examiner is authorized to charge Applicants' Deposit Account No. 19-5425 therefore.

Respectfully Submitted,

Date: September 22, 2005

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